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Computational verification of large logical models - application to the prediction of T cell response to checkpoint inhibitors

Abstract:

At the crossroad between biology and computational modelling, systems biology has proved to be an important ally to gain a mechanistic understanding of biological systems. But as our knowledge accumulates, the size and complexity of mathematical models increase, calling for the development of efficient dynamical analysis methods. In this study, we take advantage of generic computational techniques to enable the dynamical behaviour of complex cellular network models.

A first approach, called "model verification", enables the formalisation and the automated verification of validation criteria for whole models or selected subparts, thereby greatly facilitating model development and correction.

A second approach, "value percolation", enables the computation of the impact of specific environmental or genetic conditions on model dynamics.

We apply these methods to the analysis of the pathways involved in checkpoint inhibitor blockade, a domain of cancer immunotherapy under active scrutiny.

The proposed methods and models will soon be made available in the all-inclusive CoLoMoTo Docker image, which provides a reproducible modeling environment, and in an interactive companion notebook.